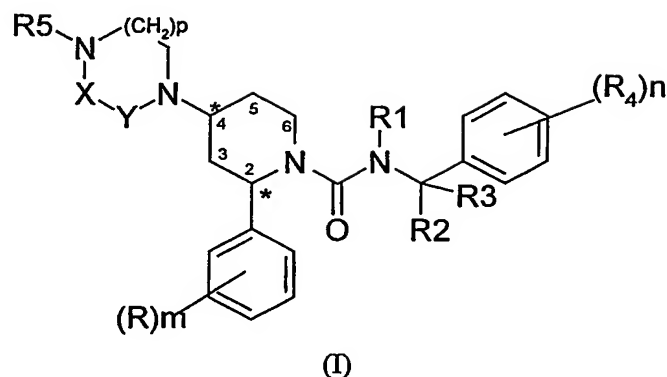


Claims

1. A compound of formula (I)



wherein

R represents halogen or C<sub>1-4</sub> alkyl;

R<sub>1</sub> represents hydrogen or C<sub>1-4</sub> alkyl;

10 R<sub>2</sub> represents hydrogen, C<sub>1-4</sub> alkyl;

R<sub>3</sub> represents hydrogen, C<sub>1-4</sub> alkyl;

R<sub>4</sub> represents trifluoromethyl, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, trifluoromethoxy or halogen;

R<sub>5</sub> represents hydrogen, C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C(O)R<sub>6</sub> or S(O)<sub>2</sub>R<sub>6</sub>;

R<sub>6</sub> represents C<sub>1-4</sub> alkyl or C<sub>3-7</sub> cycloalkyl;

15 m is zero or an integer from 1 to 3;

n is an integer from 1 to 3;

p is an integer from 1 to 2;

X and Y are independently C(O) or CH<sub>2</sub>;

provided that

20 i) X and Y are not both C(O) and

ii) when X and Y are both CH<sub>2</sub> and p is 1, R<sub>5</sub> is not hydrogen, C<sub>1-4</sub> alkyl or C(O)R<sub>6</sub>;

and pharmaceutically acceptable salts and solvates thereof.

- 25 2. A compound as claimed in claim 1 wherein R is a halogen (e.g. fluorine) and/or a C<sub>1-4</sub> alkyl (e.g. methyl) group and m is preferably zero or an integer from 1 to 2.

3. A compound as claimed in claim 1 or 2 wherein R<sub>1</sub> is a methyl group.

30 4. A compound as claimed in any claims from 1 to 3 wherein R<sub>2</sub> is a hydrogen atom or a methyl group.

5. A compound as claimed in any claims from 1 to 4 wherein R<sub>3</sub> is a hydrogen atom or a methyl group.

35 6. A compound as claimed in any claims from 1 to 5 wherein R<sub>4</sub> is a trifluoromethyl group or halogen (i.e. chlorine).

7. A compound as claimed in any claims from 1 to 6 wherein R<sub>5</sub> is hydrogen, metyl, cyclopropyl, C(O)CH<sub>3</sub> or S(O)<sub>2</sub>CH<sub>3</sub>.

8. A compound as claimed in any claims from 1 to 7 wherein p is 1.

9. A compound as claimed in any claims from 1 to 8 wherein R is at the 2 and/or 4 position in the phenyl ring.

10. A compound as claimed in any claims from 1 to 9 wherein n is 2 and the groups R<sub>4</sub> are at the 3 and 5 position in the phenyl ring.

11. A compound as claimed in any claims from 1 to 10 wherein

R is fluorine and/or C<sub>1-4</sub> alkyl (e.g. methyl);

R<sub>1</sub> is a methyl group;

R<sub>2</sub> is a hydrogen atom or a methyl group;

R<sub>3</sub> is a hydrogen atom or a methyl group;

R<sub>4</sub> is trifluoromethyl;

R<sub>5</sub> is hydrogen, metyl, cyclopropyl, C(O)CH<sub>3</sub> or S(O)<sub>2</sub>CH<sub>3</sub>;

m is 1 or 2;

n is 2;

p is 1.

12. A compound selected from

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(R)-(3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(R)-(4-methyl-3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-(3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(4-methyl-3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-(3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(4-methyl-3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(R)-(2-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(4-Fluoro-2-methyl-phenyl)-4-(S)-(2-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(4-Fluoro-2-methyl-phenyl)-4-(S)-(2-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(2-oxo-4-methyl-piperazin-1-yl)-piperidine-1-carboxylic acid, (3,5-bis-trifluoromethyl-benzyl)-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(4-methyl-2-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(4-methyl-2-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(R)-(4-cyclopropyl-3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-(3,5-bis-trifluoromethyl-benzyl)-methanamide;

5 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(4-cyclopropyl-3-oxo-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-(3,5-bis-trifluoromethyl-benzyl)-methanamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(1-methanesulfonyl-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-(3,5-bis-trifluoromethyl-benzyl)-methanamide;

10 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(1-methanesulfonyl-piperazin-1-yl)-piperidine-1-carboxylic acid, 1-[(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide;

and pharmaceutically acceptable salts (e.g. hydrochloride, methanesulphonate, sulphate, p-toluensulphonate) and solvates thereof.

13. A compound as claimed in any claims from 1 to 12 for use in therapy.

14. The use of a compound as claimed in any claims from 1 to 12 in the preparation of a medicament for use in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins.

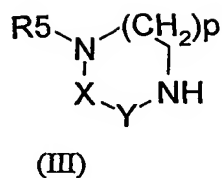
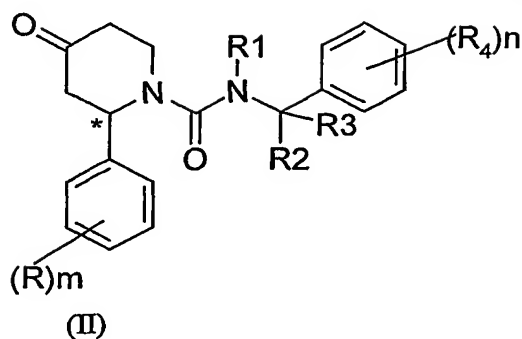
15. The use of a compound as claimed in any claims from 1 to 12 in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins.

16. A pharmaceutical composition comprising a compound as claimed in any claims from 1 to 12 in a mixture with one or more pharmaceutically acceptable carriers or excipients.

17. A method for the treatment of a mammal, including man, in particular in the treatment of conditions mediated by tachykinins, including substance P and other neurokinins, comprising administration of an effective amount of a compound as claimed in any claims from 1 to 12.

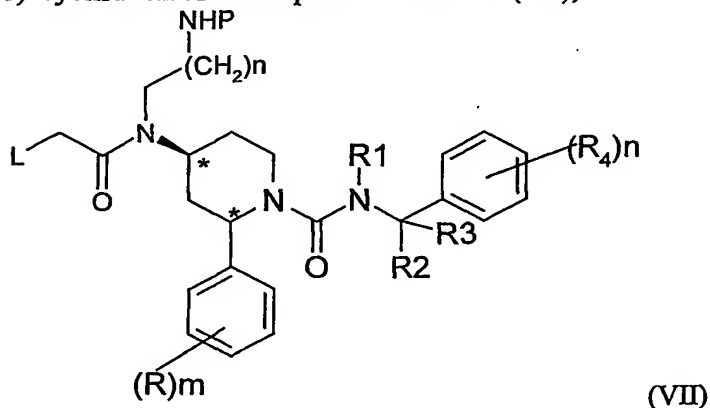
18. A process for the preparation of a compound as claimed in any claims from 1 to 12, which comprises

a) reacting a compound of formula (II),



with compound of formula(III) in the presence of a suitable metal reducing agent to prepare a compound of formula (I), wherein X is CH<sub>2</sub> or C(O) and Y is CH<sub>2</sub>;

- 5 b) cyclisation of a compound of formula (VII),



wherein P is a nitrogen protecting group and L is a suitable leaving group, to obtain compounds of formula (I) wherein Y is C(O);

followed where necessary or desired by one or more of the following steps:

- 10 i) removal of any protecting group;  
 ii) isolation of the compound as a salt or a solvate thereof;  
 iii) separation of a compound of formula(I) or derivative thereof into the enantiomers thereof.